FORM PTO-1449

SECOND SUPPLEMENTAL A TRADE INFORMATION DISCLOSURE STATEMENT

Applicant.

| ATTY. DOCKET NO. 1696.0020008/RWE/RAS | APPLICATION NO. 09/845,153 |
|--|----------------------------|
| APPLICANT Shen et al. | |
| FILING DATE | GROUP |
| May 1, 2001 | 1646 |

| | U.S. PATENT DOCUMENTS | | | | | | | | | | | |
|---------------------|-----------------------|-----------------|------|------|-------|-----------|-------------|--|--|--|--|--|
| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE | | | | | |
| | AA | | | | | | | | | | | |
| | AB | | | · | | | | | | | | |
| | AC | | | · | | | | | | | | |
| | AD | | | | | | | | | | | |
| | AE | | | | | | | | | | | |
| _ | AF | | | | - | | | | | | | |
| | AG | | | | | | | | | | | |
| | АН | | | | | | | | | | | |
| | AI | | | | | | <u> </u> | | | | | |
| | AJ | | | | | | | | | | | |
| | AK | | | | | | | | | | | |

| | | | Porbign | PATENT DOCUMENTS | | | |
|---------------------|-----|-----------------|------------|------------------|-------|-------------|-------------|
| EXAMINER INITIAL | | DOCUMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATION |
| 10 | AL2 | WO 97/49425 Al | 12/31/1997 | WIPO | | > | Yes No |
| | АМ | | | | | | Yes No |
| | AN | | | | | | Yes No |
| | AO | | | | | | Yes No |
| | AP | | | | | | Yes No |

| | | | OTHER (Including Author, Title, Date, Pertinent Pages, etc.) |
|----------|----|----|---|
| | AR | | |
| P | AS | 23 | Kiwada, H., et al., "Application of Synthetic Liposomes Based on Acyl Amino Acids or Acyl Peptides as Drug Carriers. I. Their Preparation and Transport of Glutathione into the Liver," Chem. Pharm. Bull. 35:2935-2942, Pharmaceutical Society of Japan (1987) |
| P | AT | 23 | Supplemental European Search Report for Application No. EP 97 94 4483, European Patent Office, the Netherlands, completed April 14, 2004 |
| EXAMINER | 10 | | DATE CONSIDERED 3/16/05 |
| | | | erence considered, whether or not citation is in conformance with MPEP 609. Draw line or conformance and not considered. Include copy of this form with next communication to |

Page 1 of 2

FORM PTO-1449

| FIRST | SUPPLEMENT | AL_ |
|-------------|------------|-----------|
| INFORMATION | DISCLOSURE | STATEMENT |

| ATTY. DOCKET NO. 1696.0020008/RWE | APPLICATION NO. 09/845,153 |
|--------------------------------------|----------------------------|
| APPLICANT Shen et al. | |
| FILING DATE | GROUP |

| _ | ORMATIC | N DIS | CLOSURE STATE | MENT | FILING DATE May 1, 2001 | | GROUP 1646 | - <u></u> |
|---------------------|---------|-------------|---------------|--|---|-----------------------------------|------------------------------|-----------------------------|
| | | | | U.S. PA | TENT DOCUMENTS | | | |
| EXAMINER INITIAL | | DOCII | MENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
| | AA | 1 | MENT NOMBER | DATE | NAULE | CIIASS | SUB-CEASS | FILING DATE |
| | AB | † | | | | | 1 | |
| | AC | | | İ | | | <u> </u> | <u> </u> |
| | AD | | | | | | 1 | |
| _ | AE | | | | | | | |
| | AF | | | | | | | |
| | AG | | | | | | | |
| • | AH | | | | | | <u> </u> | |
| | AI | | ····· | | | | <u> </u> | <u></u> |
| | AJ | | | | | | <u> </u> | |
| | AK | | | <u> </u> | l | | J | <u> </u> |
| | | | <u></u> | FORBIGN P | ATENT DOCUMENTS | | | |
| EXAMINER INITIAL | | DOCU | MENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATIO |
| | AL | | | | | | | Ye N |
| | AM | | | | | | | Ye N |
| | AN | | | | | | | Ye N |
| | AO | <u></u> | | | | | | Ye N |
| AP_ | AP1 | WO 9 | 0/10621 A1 | 09/20/1990 | WIPO | | | Ye N |
| | | OT | HER (Includir | g Author, Ti | tle, Date, Pertinent | Pages, etc | 2.) | |
| | AR | | | | | | | |
| 40 | AS | 22 | Conjugates o | ., et al., "S f a Cyclic La mical Society | Synthesis and Biolog: actam α -Melanotropin, γ (1992) | ical Activi ," <i>J. Med</i> . | ties of Fatt Chem. 35:118 | ty Acid 3-123, |
| P | AT | 22 | for reversib | le lipidizat: | ater-soluble fatty action of polypeptides" (September 1995) | cid derivat FEBS Lett. | ives as acy: 371:283-286 | lating agent 5, Elsevier |
| EXAMINER | 1 | Va. | y | ······································ | | DATE | CONSIDERED | 3/16/05 |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

Page 2 of 2

SE 26 THE STATE OF THE SERVICE OF THE PROPERTY
FORM PTO-1449

FIRST SUPPLEMENTAL INFORMATION DISCLOSURE STATEMENT

| ATTY. DOCKET NO. 1696.0020008/RWE | APPLICATION NO. 09/845,153 |
|--------------------------------------|----------------------------|
| APPLICANT Shen et al. | |
| FILING DATE | GROUP |

| | | | | | May 1, 2001 | | 1646 | |
|---------------------|---------------------------------------|----------------|---------------------------------------|---------------------------------------|---------------------------------------|---------------------------------------|-------------|--------------------|
| | | | | U.S. PA | ATENT DOCUMENTS | | | |
| EXAMINER INITIAL | | DOC | JMENT NUMBER | DATE | NAME | CLASS | SUB-CLASS | FILING DATE |
| • | AA | | | | | | | |
| | AB | | | | | | N - | |
| | AC | | | | | | MEC | |
| | AD | | | | | | | FIVEN |
| | AE | | • | | | | SEP . | 2003 |
| | AF | | | | | 77 | | 2007 |
| • | AG | | | <u> </u> | i | 1/2 | UP CEATTER | |
| • | AH | | | | | | Harri | 600/20- |
| | AI | | | 1 | | | CH CENTER | 2012900 |
| | AJ | | | | | | | |
| | AK | | | | | | | |
| | · · · · · · · · · · · · · · · · · · · | | | FORBIGN | PATENT DOCUMENTS | · · · · · · · · · · · · · · · · · · · | | * |
| EXAMINER | | | | | | | | |
| NITIAL | | DOCU | JMENT NUMBER | DATE | COUNTRY | CLASS | SUB-CLASS | TRANSLATIO |
| | AL | | | | | | | Ye |
| • | AL | +- | · · · · · · · · · · · · · · · · · · · | } | | | + | N N |
| | АМ | ŀ | | | | | | Ye |
| | | 1 | | · · · · · · · · · · · · · · · · · · · | | | 1 | Ye |
| | AN | <u> </u> | | | | | | N |
| | 1 | | | • | | |] | Ye |
| | AO | + | | | | | + | N |
| | AP | | | | | | 1 | Ye N |
| | - 1 | 0' | THER (Includin | g Author, T | itle, Date, Pertine | ant Pages, etc | g.) | <u> </u> |
| 10 | AR | 23 | European Sea July 2, 2003 | rch Report i | for European Patent | Application | No. 03 00 6 | 780 mailed o |
| | AS | | | | | | | · |
| | AT | | | | | | | |
| XAMINER | 10 | $ \leftarrow $ | | | · · · · · · · · · · · · · · · · · · · | DATE | CONSIDERED | 2/1//5= |
| | | _ | | | | Invie | COMPTDEKED | CILLIA |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

TLULIVLU

AUG 2 8 2001

TECH CENTER 1600/2900

AUG 2 3 2000

Page 1 of 22 APPLICATION NO TRAD ATTY. DOCKET NO. 09/845,153 1696.0020008/RWE/BEC FORM PTO-1449 APPLICANTS AUG 2 7 2001 Shen et al INFORMATION DISCLOSURE STATEMENT GROUP FILING DATE 1646 May 1, 2001 U.S. PATENT DOCUMENTS EXAMINER CLASS SUB-FILING DATE NAME DOCUMENT DATE INITIAL CLASS NUMBER 09/24/1993 530 331 02/04/1997 Kauvar et al. 5,599,903 AA1 04/22/1994 424 489 Leone-Bay et al. 05/13/1997 5,629,020 AB1 01/18/1994 435 172.3 06/03/1997 Naftilan et al. 5,635,380 AC1 05/31/1994 514 18 Kauvar et al. 10/21/1997 AD1 5,679,643 06/06/1995 387.3 530 01/13/1998 Willner et al. 5,708,146 AE1 06/07/1995 331 530 Kauvar et al. 06/09/1998 5,763,570 AF1 AG AΗ ΑI ΑJ AK FOREIGN PATENT DOCUMENTS TRANSLATION EXAMINER SUB-CLASS COUNTRY DATE DOCUMENT INITIAL CLASS NUMBER Abstract Yes No Japan JP 63246382 10/13/1988 AL1 Yes No WIPO 10/31/1991 WO 91/16067 AM1 Yes No Europe EP 0 482 766 04/29/1992 AN1 Yes No WIPO 08/01/1996 WO 96/22773 A01 Yes No AP OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Artursson, P., and Magnusson, C., "Epithelial Transport of Drugs in Cell Culture. II: Effect of Extracellular Calcium Concentration on the Paracellular Transport of Drugs of Different Lipophilicities across Monolayers of Intestinal AR 1 Epithelial (Caco-2) Cells, J. Pharm. Sci. 79:595-600, American Pharmaceutical Association (1990). Broadwell, R.D., et al., "Transcytotic pathway for blood-borne protein through the blood-brain barrier," Proc. Natl. Acad. Sci. USA 85:632-636, National Academy AS 1 of Sciences (1988). Brocklehurst, K., et al., "Preparation of Fully Active Papain From Dried Papaya Latex," Biochem. J. 133:573-584, London Portland Press On Behalf Of The AΤ <u>1</u> Biochemical Society (1973). DATE CONSIDERED EXAMINER

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPED 609. line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

AUG 2 8 2001

| PORM PTO-1449 INFORMATION DISCLOSURE STATES FRANCE See et al. See . 0.02000/1878/36 See . 0.02000/1878/3 | FORM PTO-1449 INFORMATION DISCLOSURE STATE PRACTICE SHEET AND STATES OF THE STATE | | | | | OIPE | | | | · ACNITED | +GARIMORA 22 |
|--|--|-------------------|-------------|----------------|-------------------------------|---|---|---|--|--|--|
| MINTER DOCUMENT NUMBER DOCUMENT NUMBER AB AB AB AB AB AB AB AB AB A | INFORMATION DISCLOSURE STATES TRANSPORT TO THE PROPERTY OF THE | | | | | / | (4) | | | | |
| INFORMATION DISCLOSURE STATE TRANSPORT TRANSPORT TRANSPORT TRANSPORT TO THE TRANSPORT | THEORYATION DISCLOSURE STATES TRADE TO THE PROPERTY OF THE STATES TO THE | | • | | | MIR 5 3 5004 | 1ATTY. DOCKET NO 21696.0020008/RW | E/BEC | 09/84 | 5,15 | · |
| DOCUMENT NUMBER DATE NAME CLASS SUBCLASS MINITIAL DOCUMENT NUMBER DATE NAME CLASS SUBCLASS AA AA AB AC | TILL DOCUMENT DATE NAME CLASS SUBCLASS FILING DATE NUMBER DATE NUMBER CLASS SUBCLASS | | FC | ORM PT | 0-1449 | 12 | APPLICANTS | <u>F</u> A | i. 81 naa | | |
| DOCUMENT NUMBER DATE NAME CLASS SUBCLASS MINITIAL DOCUMENT NUMBER DATE NAME CLASS SUBCLASS AA AA AB AC | TILL DOCUMENT DATE NAME CLASS SUBCLASS FILING DATE NUMBER DATE NUMBER CLASS SUBCLASS | INFO | RMATION | DISCI | OSURE ST | ATHOMIT PAREMAR | | AUE | , - 1 - 100 | _ | |
| MANNER DOCUMENT NUMBER AA AB AC AD AC AD AC AB AF AF AG AH AI AI AI AN DOCUMENT NUMBER CLASS SUB-CLASS FILING DATE CLASS SUB-CLASS FILING DATE FILING DATE CLASS FILING DATE CLASS FILING DATE FILING DATE CLASS SUB-CLASS TRANSLATIO CLASS SUB-CLASS TRANSLATIO CLASS CLASS TRANSLATIO CLASS TRANSLATIO CLASS TRANSLATIO CLASS TRANSLATIO CLASS TRANSLATIO CLASS CLASS TR | MINER NOWBER DATE NAME CLASS SUB-CLASS FILING DATE NOWBER CLASS FILING DATE NOWBER CLASS FILING DATE CLASS FILING DATE CLASS SUB-CLASS FILING DATE CLASS SUB-CLASS FILING DATE CLASS SUB-CLASS SUB-C | | | | | THINK! | | | 1545 | Δ | |
| DATE NAME CLASS CLASS AA AR AR AC AC AD AE AF AG AF AG AH AI AI AI AI AI AN AN AN AN AN | DATE NAME DOCUMENT NUMBER AA AB AC AC AC AC AC AC AC AC | | | | | U.S. | PATENT DOCUMENTS | 77 | 7 170 | , | |
| DATE NAME CLASS CLASS AA AR AR AC AC AD AE AF AG AF AG AH AI AI AI AI AI AN AN AN AN AN | DATE NAME DOCUMENT NUMBER AA AB AC AC AC AC AC AC AC AC | AMINER | T | | | | | | CLASS | erm_ | FILING DATE |
| AA AB AC AC AD AE AF AF AG AN AN AN AN AN AN AN AN AN | AA AB AC AC AD AB AC AD AB AF AF AG AG AG AN AI AI AJ AI AJ AK PORRIGH PATENT DOCUMENTS CLASS SUB- CLASS SUB- CLASS TRANSLATIO CLA | ITIAL | | | | DATE | NAME | | CIASS | | |
| AB AC AD AC AD AB AE AF AG AG AH AI AI AI AI AN AR PORMIGN PATENT DOCUMENTS CLASS SUB- CLASS | AE AC AD AD AE AF AF AF AF AF AG AN AH AI AI AI AI AN AN BOUWENT TIAL DOCUMENT NUMBER DATE COUNTRY CLASS SUB- CLASS TRANSLATIO CLASS VI AM AN AN AN AN AN AN AN AN AN | | | NOMBE | | | | | | | |
| AC AD AE AF AF AG AN AN AT AJ AK PORRIGN PATENT DOCUMENTS CAMINER DOCUMENT NUMBER DOCUMENT NUMBER AN AN AN AN AN AN AN AN AN A | AC AD AE AF AG AN AI AI AJ AX POREIGN PATENT DOCUMENTS FOREIGN PATENT DOCUMENTS CLASS SUB- CLASS TRANSLATIO CLASS Y AL AM AN AN AN AN AN AN AN AN AN | | | | | | | | <u> </u> | | |
| AE AF AG AG AH AI AI AJ AX FOREIGN PATENT DOCUMENTS CLASS SUB- CLASS TRANSLATIO CLASS CLASS Y AL AN AN AN AN AN AN AN AN AN | AE AF AG AG AH AI AJ AJ AX FOREIGN PATENT DOCUMENTS CLASS SUB- CLASS SUB- CLASS TRANSLATIO CLASS SUB- CLASS TRANSLATIO TRANS | | | | | | | | | | |
| AF AG AH AI AI AJ AX FOREIGN PATENT DOCUMENTS CAMINER NITIAL DOCUMENT NUMBER AL AM AN | AP AG AH AI AI AJ AJ AK FOREIGN PATENT DOCUMENTS MINER TIAL DOCUMENT DATE COUNTRY CLASS SUB- CLASS TRANSLATIO CLASS TRANS | | AD | | | | | | | | |
| AG AH AI | AR AND | | AE | | | | | | - - | | |
| AH AI AJ AK FOREIGN PATENT DOCUMENTS AL AM AN AN AN AN AN AP OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). AS 2 Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). EXAMINER DATE CONSIDERED J. U.S. DAT | AH AI AJ AJ AN AN FOREION PATENT DOCUMENTS MINIER TIAL DOCUMENT DATE COUNTRY CLASS SUB-CLASS TRANSLATIO CLASS TRANSLATIO Y AL AN AN AN AN AO CHER (Including Author, Title, Date, Pertinent Pages, etc.) Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). AS 2 Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). CAMINER: Initial if reference considered, whether or not citation is in conformance with MPEF 509. Date CONSIDERED J. LASS LAMINER: Initial if reference considered, whether or not citation is in conformance with MPEF 509. Date of this form with next | | AF | | | | | | 1 | 1 | |
| AI AJ AX FOREIGH PATENT DOCUMENTS CAMINER NITIAL DOCUMENT NUMBER DOTHER (Including Author, Title, Date, Pertinent Pages, etc.) OTHER (Including Author, Title, Date, Pertinent Pages, etc.) AR Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). AS Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). | AX AX POREIGN PATENT DOCUMENTS MINNER TIAL DOCUMENT DATE COUNTRY CLASS SUB- TRANSLATIO CLASS Y AL AN AN AN AN AN AN AN AN AN | | AG | | | | | | 1 | | |
| AMINIER NOTHER (Including Author, Title, Date, Pertinent Pages, etc.) AR 2 Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). AS 2 Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). EXAMINER DATE CONSIDERED JUBS DA | MINER TIAL DOCUMENT DATE COUNTRY CLASS SUB-CLASS AL AN AN AN AN AN AN AN AN AN | | AH | | | + | | | | 1 | |
| TAMINER TOTHER (Including Author, Title, Date, Pertinent Pages, etc.) AR Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). AS Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Blochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). | MINITER DOCUMENT DATE COUNTRY CLASS SUB-CLASS TRANSLATION AL AM AN AN AO AP OTHER (Including Author, Title, Date, Pertinent Pages, etc.) AR Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). AS Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). CAMINER: Initial if reference considered, whether or not citation is in conformance with Myes 609. Date CONSIDERED SUMMANTER: Initial if reference considered, whether or not citation is in conformance with Myes 609. Date CONSIDERED SUMMANTER: Initial if reference considered, whether or not citation is in conformance with Myes 609. Date CONSIDERED SUMMANTER: Initial if reference considered, whether or not citation is in conformance with Myes 609. Date CONSIDERED SUMMANTER: Initial if reference considered, whether or not citation is in conformance with Myes 609. Date CONSIDERED SUMMANTER: Initial if reference considered, whether or not citation is in conformance with Myes 609. Date CONSIDERED SUMMANTER: Initial if reference considered, whether or not citation is in conformance with Myes 609. Date CONSIDERED SUMMANTER: Initial if reference considered, whether or not citation is in conformance with Myes 609. Date CONSIDERED SUMMANTER: Initial if reference considered, whether or not citation is in conformance with Myes 609. Date CONSIDERED SUMMANTER: Initial if reference considered in conformance and not considered. Include copy of this form with next | | AI | | | | | | | | |
| AL AN OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). AS 2 Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Blochem. 33:13087-13092, American Chemical Society (1994). EXAMINER DATE CONSIDERED SLUGS DATE CONSIDERED SLUGG DATE CONSIDERED SLUGG DATE CONSIDERED SLUGG DATE CONSIDERED SLUGS DATE CONSIDERED SLUGG DATE | MINER DOCUMENT DATE COUNTRY CLASS SUB-CLASS TRANSLATION CLASS ALL PROPERTY NUMBER DATE COUNTRY CLASS SUB-CLASS TRANSLATION CLASS ALL PROPERTY NUMBER DATE COUNTRY CLASS SUB-CLASS TRANSLATION CLASS ALL PROPERTY NUMBER ALL PROPER | | | ┼ | | | | | | | |
| DOCUMENT DATE COUNTRY CLASS SUBCLASS TRANSLATIO AL AM AN AN OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). AS 2 Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. J3:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). | MINER TIAL DOCUMENT NUMBER COUNTRY CLASS SUB-CLASS TRANSLATION CLASS SUB-CLASS SUB | | AK | | | FOREI | GN PATENT DOCUMENT | rs | | | |
| DOCUMENT NUMBER DATE COUNTRY CLASS CLASS Y. AL AM AN AN AN AO CHER (Including Author, Title, Date, Pertinent Pages, etc.) Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). AT Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). EXAMINER DATE CONSIDERED S/LUSS | DOCUMENT NUMBER AL AL AM AN AN AN AO Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). AS Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (November 1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). CAMMINER: Initial if reference considered, whether or not citation is in conformance with MPEF 609. Diese through citation if not in conformance and not considered. Include copy of this form with next | | | т | | | | • | | C.m. | TRANSLATIO |
| AM AN AN AN AN AN AN AN AN AN | AM AN AN Y AN AN Y AN AN Y Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Blochem. 33:13087-13092, American Chemical Society (1994). AT 2 Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). XAMINER: Initial if reference considered, whether or not citation is in conformance with MPEF 609. Date considered in those of the period of the peri | KAMINER NITIAL | | 1 | | DATE | COUNTRY | | CLASS | | |
| AM AN AN AN AN AN AN AN AN AN | AM AN AN AN AN AN AN AN AN AN | | | Ţ | _ | ļ | | | _ | | 1 |
| AM AN AN AN AN AN AN AN AN AN | AM AN AN AN AN AN AN AN OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). AT Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). CAMMINER: Initial if reference considered, whether or not citation is in conformance with MPEF 609. Dies through citation if not in conformance and not considered. Include copy of this form with next | | AL | | | | | | | | Ye |
| AN AP OTHER (Including Author, Title, Date, Pertinent Pages, etc.) AR Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). EXAMINER DATE CONSIDERED SULTS DATE CONSIDERED | AN AD OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). XAMINER: Initial if reference considered, whether or not citation is in conformance with MPEF 609. Dine through citation if not in conformance and not considered. Include copy of this form with next | | AM | <u> </u> | | | | | | + | |
| OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). | OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). AS 2 Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). CAMMINER: Initial if reference considered, whether or not citation is in conformance with MPEF 609. Digite through citation if not in conformance and not considered. Include copy of this form with next | | | | | | | | | | 1 |
| AR 2 Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). | AP OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). CAMMINER: Initial if reference considered, whether or not citation is in conformance with MPEF 609. Digite through citation if not in conformance and not considered. Include copy of this form with next | | AN | + | | | | | | | Y |
| OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 2465829, American Chemical Society (November 1994). EXAMINER | OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). CAMMINER: Initial if reference considered, whether or not citation is in conformance with MPEF 609. Digite through citation if not in conformance and not considered. Include copy of this form with next | | AO | | | | | | | | |
| Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). | AR 2 Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). AS 2 Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). XAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Dine through citation if not in conformance and not considered. Include copy of this form with next | | | | | | | | | | |
| Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). AS 2 Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). AT 2 Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). | Chekhonin, V.P., et al., "Fatty acid acylated Fab-fragments of antibodies to neurospecific proteins as carriers for neuroleptic targeted delivery in brain," FEBS Letters 287:149-152, Elsevier Science Publishers B.V. (1991). AS 2 Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). XAMINER: Initial if reference considered, whether or not citation is in conformance with MPEF 609. Dine through citation if not in conformance and not considered. Include copy of this form with next | | AP | | | North and Austria | - Title Date Pe | rtinent Pa | ges, etc. |) | |
| AR 2 neurospecific proteins as Califers Science Publishers B.V. (1991). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 2465829, American Chemical Society (November 1994). EXAMINER DATE CONSIDERED SILVES DATE CONSIDERED SILVES DATE CONSIDERED SILVES | AR 2 neurospecific proteins as carriers for medical for medical science Publishers B.V. (1991). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Biochem. 33:13087-13092, American Chemical Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 2465829, American Chemical Society (November 1994). XAMINER DATE CONSIDERED SULUS XAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Dine through citation if not in conformance and not considered. Include copy of this form with next | | | | OTHER (I | ncluding Author | r, riche, bace, | | | | |
| Amphioxus Insulin-like Peptide, Blothem. Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). EXAMINER DATE CONSIDERED SULUS | Amphioxus Insulin-like Peptide, Brothem. Society (1994). Chu, YC., et al., "High-Potency Hybrid Compounds Related to Insulin and Amphioxus Insulin-like Peptide," Chem. Abstracts 121:212, Abstract No. 246582y, American Chemical Society (November 1994). XAMINER DATE CONSIDERED SULUS EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Dine through citation if not in conformance and not considered. Include copy of this form with next | P | AR | 2 | Chekhon neurosp FEBS Le | in, V.P., et a ecific protein etters 287:149- | 1., "Fatty acid ac s as carriers for 152, Elsevier Scie | cylated Fal neurolept ence Publia | o-fragment ic targete shers B.V. | s of anti d deliver (1991). | bodies to ry in brain," |
| Amphioxus Insulin-like Peptide, "Chem. Abstracts 121.000 American Chemical Society (November 1994). EXAMINER DATE CONSIDERED SILVES DATE CONSIDERED SILVES EXAMINER | Amphioxus Insulin-like Peptide, Chem. Abstracts 121.11. American Chemical Society (November 1994). DATE CONSIDERED SULUS EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Direct through citation if not in conformance and not considered. Include copy of this form with next | R | AS | 2 | Amphio | cus Insulin-lik | High-Potency Hybr se Peptide," Bioch | id Compoun em. 33:130 | ds Relateo 87-13092, | l to Insul American | lin and Chemical |
| EXAMINER S/C405 | XAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Dispersion of the conformance and not considered. Include copy of this form with next ine through citation if not in conformance and not considered. | P | AT | 2 | | a Inculin-lil | ke Pentide." Chem. | ADSLIACES | ds Relate : 121:212, | d to Insu Abstract | lin and No. 246582y, |
| in the in conformance with MPEP 609. I | XAMINER: Initial if reference considered, whether or not citation is in conformance with MPEF 609. Do not citation if not in conformance and not considered. Include copy of this form with next ine through citation if not in conformance and not considered. | | | \ - | | | | | DATE CO | NSIDERED, | 2/1/05 |
| EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 002. | ine through citation if not in conformance and not simple through | | _1K | 4 | کے | | | | | anga with | MPER 609. D |
| | ine through citation if not in conformance and not consormance and | EXAMINER: | Initia | il if | reference | e considered, v | whether or not cit | ation is i . Include | n conform | this form | with next |

ANC 5 8 5001 TECH CENTER 1600/2900

Page 3 of 22

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

EXAMINER

EXAMINER

INITIAL

INITIAL

ATTY. DOCKET NO. 1696.0020008/RWE/BEC APPLICATION NO. 09/845,153

APPLICANTS Shen et al. AUG 2 7 2001

FILING DATE May 1, 2001 U.S. PATENT DOCUMENTS FILING DATE CLASS SUB-NAME DATE DOCUMENT CLASS NUMBER AA AΒ AC ΑD ΑE AF AG AH ΑI ΑJ AK FOREIGN PATENT DOCUMENTS TRANSLATION CLASS SUB-COUNTRY DATE DOCUMENT CLASS NUMBER Yes No AL Yes No AM Yes No AN Yes No ΑO Yes No AP OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Conradi, R.A., et al., "The Influence of Peptide Structure on Transport Across Caco-2 Cells," Pharm. Res. 8:1453-1460, Plenum Publishing Corp. (1991). AR <u>3</u> Edwards, P.A.W., "Is Mucus a Selective Barrier to Macromolecules?" British Med. AS <u>3</u> Bulletin 34:55-56, British Council, Medical Dept. (1978).

EXAMINER

ΑT

<u>3</u>

DATE CONSIDERED

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

Arbor, MI, i-xiii, 9-226 (after January 25, 1995)

Ekrami, H.M., "Positively-charged and lipophilic Bowman-Birk Protease Inhibitor conjugates: Synthesis and Characterization of the Pharmaceutical and Chemopreventive properties," A Dissertation, UMI Dissertation Services, Ann

AUG 2 8 2001

TRAN 1696.0020008/RWE/BEC

APHICATION NO. 09/845, 153

| | | ORM PTO | | | APPLICANTS Shen et al. | RE | | | |
|---------------------|----------|--------------|------------|---|--|---|----------------------------------|-----------------------------------|---|
| INFOR | MOITAM | DISCL | OSURE STA | <u>rement</u> | FILING DATE May 1, 2001 | AU | G & 1646 | 01 | · · · · · · · · · · · · · · · · · · · |
| | | | | U.S. | PATENT DOCUMENTS | | 170 | 20 | |
| EXAMINER INITIAL | | DOCUM | | DATE | NAME | | CLASS | SUB- CLASS | FILING DATE |
| | AA | | | | | | | | |
| | AB | | | | | | | | |
| | AC | | | | | | | | |
| | AD | ļ | | | | | | | |
| | AE | ↓ | | | | | | <u> </u> | |
| | AF | ↓ | | | | | | | |
| | AG | ↓ | | | | | | | |
| | AH | | | | | | | | |
| | AI_ | + | | | | | | | |
| | AJ AK | ╁╌╴ | | | | | | | |
| | AX | | | FOREI | GN PATENT DOCUMENTS | | <u>,</u> | | |
| EXAMINER INITIAL | | DOCU | MENT | DATE | COUNTRY | | CLASS | SUB- CLASS | TRANSLATION |
| | ├ | NUMB | ER | | | | } | 1 | Ye: |
| | AL | | | | - | | | + | Ye |
| | T | | | İ | | | <u> </u> | | N |
| | AM - | - | | + | , | | | | Ye N |
| | AN | | | | | | | + | Ye |
| | | _ i | | | | | | | N- |
| | AO | +- | | | | | | | Ye N |
| 1 | AP | | | | | | | | |
| | | (| OTHER (Inc | luding Author | r, Title, Date, Pertin | nent Pag | es, etc.) | | |
| P | AR | 4 | | | "Water-soluble fatty zation of polypeptide n Biochemical Societion | 3, 100 | , 20000- | s as acyl 371:283- | ating agents 286, |
| \sim | AS | 4 | C | -aible linidi | "Water-soluble fatty zation of polypeptide Chemical Society (199 | , ,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,,, | erivative Abstract | s as acyl s 124:104 | ating agents 2, Abstract |
| 10 | 1 | | | | | | | | |
| 100 | AT | 4 | enzyme-c | s, S.A., and Matalyzed thic arboxy-4-nitro | Mannervik, B., "A meth ol-disulfide interchan obezenethiol," Biochim | nod for nge usin m. Bioph | the direct g mixed days. Acta | t recordi isulfide 212:518- | ing of an of glutathion 520, Elsevier |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

AUG 2 8 2001 **TECH CENTER 1600/2900**

Page 5 of 22

FORM PTO-1449

APPLICATION NO. DOCKET NO. 197845;193 num-APPLICANTS Shen et al.

| | | | nerros con | TEMENT | Shen et al. | AUG 2 | 2001 | | |
|---------------------|--|----------------|---|--|---|--|-------------------------------------|--|--|
| INFOR | MATION | DISCLO | OSURE STA | 1EMENI | FILING DATE | GROUP 1646 | GROUP 2001 | | |
| | | | = | | May 1, 2001 | TOT | 700 | | |
| | | | | บ.ร. | PATENT DOCUMENTS | | | | |
| CAMINER NITIAL | | DOCUM NUMBE | | DATE | NAME | CLASS | SUB- CLASS | FILING DATE | |
| | AA | | | | | | | | |
| | AB | | | | | | | | |
| | AC | | | | | | | | |
| | AD | | | | | | | | |
| | AE | | | | | | | | |
| | AF | <u> </u> | | | | | | | |
| | AG | <u> </u> | | | | | | | |
| | НА | <u> </u> | | | | | | | |
| | AI | | | | | | | | |
| | AJ | | | | | | | | |
| | AK | <u> </u> | | | DOCUMENTS | | | | |
| | | | | FOREI | GN PATENT DOCUMENTS | | | | |
| EXAMINER INITIAL | | | MENT | DATE | COUNTRY | CLASS | SUB- CLASS | TRANSLATION | |
| | | NUMB | ER | | | | | Yes | |
| | AL | 1 | | | | | | Ye | |
| | | | | | | | | N | |
| | AM | | | | | | | Ye | |
| | | 1 | | 1 | | | | N Yo | |
| | AN | | | | | | | Ye N | |
| | AO | | | | | | | Ye | |
| | | | | | | | | N | |
| | AP | | | | or, Title, Date, Pertine | ent Pages, etc. |) | | |
| | | | OTHER (In | cluding Autho | r, ficts, bace, teres | | | | |
| | AR | <u>5</u> | Erikssor disulfic nitrober Society | le interchange zenethiol," <i>Cl</i> | nervik, B., "Direct reco e using a mixed disulfic hem. Abstracts 73:39, Ab | ording of an er de of glutathic bstract No. 12 | nzyme-catone and 3 7175y, Am | alyzed thiol- -carboxy-4- erican Chemica | |
| \sim | AS | <u>5</u> | gastroi | A., et al., ". ntestinal tra (1986). | Acylcarnitines: drug ab ct," Am. J. Physiol. 25 | sorption-enhan 1:G332-G340, A | cing agen merican F | ats in the Physiological | |
| 10 | ı | | | | | | | | |
| 10 | AT | <u>5</u> | Barrier | via the Tran | llus, L.R., "Transport Consferrin Receptor," In: and Its Regulation, L.R. York, USA. pp.129-136 | Drewes and A. (1993). | coss the I erebral ' L. Betz, | eds. Plenum | |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. SAMMINDE: INITIAL IL reference considered, whether or not citation is in conformance with MPEP 809. line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

AUG 2 8 2001

F. TECH CENTER 1600/2900.

MAR S 3 SOON

TRADEN 1696.0020008/RWE/BEC

APPLICATION NO.

FORM PTO-1449

APPLICANTS Shen et al.

| | | | | п е | PATENT DOCUMEN | ATS | | | |
|-------------------|----|------------------|---|--------------------------------|------------------------------------|----------------|--|---------------|---------------------|
| | | | | T | PATENT DOCUMENT | 110 | | | T |
| AMINER ITIAL | | DOCUME NUMBER | | DATE | NAME | | CLASS | SUB- CLASS | FILING DATE |
| | AA | | | <u></u> | | | | | |
| | AB | | | | | | } | + | + |
| | AC | | | | | | | | + |
| | AD | | | | | | | + | + |
| | AE | I | | | | | | | |
| | AF | | | | | | | + | |
| | AG | | | | | | | 1 | |
| | АН | | | | + | | 1 | | |
| | AI | | | | | | | | |
| | UA | | | | | | 1 | | |
| | AK | | | | IGN PATENT DOCU | YOUTS | | | |
| | | | | YORE. | IGN PATENT DOCU. | ABRED | T | | T |
| (AMINER NITIAL | | DOCUM | | DATE | COUNTRY | | CLASS | SUB- CLASS | TRANSLATION |
| | + | 100 | <u> </u> | | | | 1 | | Ye |
| | AL | | | | | | + | | Ye |
| | AM | | | - | | | + | + | Y |
| | AN | | | | | | - | + | Y |
| | AO | | | | | | + | | Y |
| | AP | Ì | | | | | | | |
| | | | TURR (II | scluding Author | or, Title, Date. | , Pertinent Pa | ges, etc. |) | |
| | AR | <u>6</u> | Gonzale: Cells (| z-Mariscal, L MDCK)," J. Me | ., et al., "Tig mbrane Biol. 86 | ht Junction Fo | ermation i | n Culture | ≥d Epithelial). |
| (M) | AS | | Gordon, G.S., et al., "Nasal absorption of insulin: Enhancement by hydrophobic bile salts," Proc. Natl. Acad. Sci. USA 82:7419-7423, National Academy of Sciences (1985). | | | | | | |
| M | AT | <u>6</u> | Hashimoto, M., et al., "Synthesis of Palmitoyl Derivatives of Insulin and Their Biological Activities," Pharm. Res. 6:171-176 Plenum Press (1989) | | | | | | |
| | | | i | | | | | NSIDERED | 5/11/ |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

AUG 2 8 2001

AUR 2 7 "TECH CENTER 1609/2900

AND 2 3 MIN WE

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

| ATTY. DOCKET NO. 1696.0020008/RWE/BEC | APPLICATION NO. |
|--|-----------------|
| APPLICANTS Shen et al. | |
| PILING DATE | GROUP |

| TNEC | DMATTON | DISC | LOSURE STA | TEMENT | Shen et al. | | · | | |
|---------------------|---------|--------------|-------------------------------------|---|---|-------------|--------------------|--|-----------------------|
| INFO | RHIIOI | DIGE | 521 | | FILING DATE May 1, 2001 | | GROUP 1646 | | |
| | | | | v.s. | PATENT DOCUMENTS | | | | |
| EXAMINER INITIAL | | DOCUI | | DATE | NAME | c | LASS | SUB- CLASS | FILING DATE |
| | AA | | | | | | | | <u> </u> |
| | AB | | | | | | | | |
| | AC | | | | | | | <u> </u> | |
| | AD | | | | | | | | |
| | AE | | | | | | | - | |
| | AF | | | | | | | | |
| | AG | _ | | | | | | | |
| | AH | \downarrow | | | | | | | |
| | AI | ļ | | | | | | | |
| | AJ_ | — | | | | | | | |
| | AK | | | | | | | <u> </u> | |
| | | | | FOREIG | N PATENT DOCUMENTS | | | | |
| EXAMINER INITIAL | | DOCU | MENT ER | DATE | COUNTRY | c | LASS | SUB- CLASS | TRANSLATION |
| | AL | | | | | | | | Yes No Yes |
| | АМ | | <u></u> | | | | | <u> </u> | No Yes |
| | AN | _ | | | ļ <u></u> | | | ļ | No Yes |
| | AO | | | | | | | <u> </u> | No Yes |
| | AP | | | | | | | | No |
| | | | THER (Inc. | luding Author | , Title, Date, Pertine | nt Pages | , etc.) | | |
| \mathcal{N} | AR | 7 | Huang, W. Immunogen Ltd. (199 | and Syntheti | pophilic Multiple Anti c Vaccine, Mol. Immun | gen Pept | ide Sys 191-119 | tem for E 9, Elsevi | Peptide er Science |
| M | AS | 2 | Conjugate | ighes, R.A., et al., "Lipidic Peptides. III: Lipidic Amino Acid and Oligomer injugates of Morphine," <i>J. Pharm. Sci. 80:</i> 1103-1105, American Pharmaceutical isociation (1991). | | | | | |
| NO | AT | 7 | Conjugate | Aughes, R.A., et al., "Lipidic Peptides. V: Penicillin and Cephalosporin Acid Conjugates with Increased Lipophilic Character," J. Pharm. Sci. 81:845-848, American Pharmaceutical Association (1992). | | | | | |
| EXAMINER | M | 5 | | | | D | ATE CONS | SIDERED | 1/6/15 |
| L | | | | | | | | 7 | |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

Draw

AUG 2 8 2001

TECH CENTER 4 60009000 ADPLICATION NO. Y. DOCKET NO. 09/845,153 1696.0020008/RWE/BEC

FORM PTO-1449 APPLICANTS Shen et al. INFORMATION DISCLOSURE STATEMENT GROUP FILING DATE 1646 May 1, 2001 PATENT DOCUMENTS U.S. FILING DATE SUB-EXAMINER CLASS DATE NAME DOCUMENT CLASS INITIAL NUMBER AA AB AC ΑD ΑE AF AG ΑН ΑI ΑJ AK FOREIGN PATENT DOCUMENTS TRANSLATION CLASS SUB-EXAMINER COUNTRY DATE DOCUMENT CLASS INITIAL NUMBER No AL Yes No AΜ Yes No AN Yes No AO Yes No ΔP OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Inagaki, M., et al., "Macromolecular permeability of the tight junction of the human nasal mucosa," Rhinology 23:213-221, International Rhinologic Society AR 8 (1985). Kabanov, A.V., et al., "Lipid modification of proteins and their membrane transport, Protein Engineering 3:39-42, IRL Press (1989) AS 8 Kajii, H., et al., "Fluorescence Study on the Interaction of Salicylate with Rat Small Intestinal Epithelial Cells: Possible Mechanism for the Promoting Effects of Salicylate on Drug Absorption In Vivo, " Life Sci. 37:523-530, Pergamon Press AT 8 Ltd. (1985). DATE CONSIDERED EXAMINER

Initial if reference considered, whether or not citation is in conformance with MPEP/609. line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

CH CENTER 1600/2909 7 2007

FORM PTO-1449

APPRICATION NO. TRADE ATTY. DOCKET NO. 45,153 1696.0020008/RWE/BEC

> APPLICANTS Shen et al.

INFORMATION DISCLOSURE STATEMENT GROUP FILING DATE 1646 May 1, 2001 PATENT DOCUMENTS FILING DATE SUB-EXAMINER CLASS DATE NAME DOCUMENT CLASS INITIAL NUMBER AA AB AC ΑD ΑE AF AG AН ΑI ΑJ AΚ FOREIGN PATENT DOCUMENTS TRANSLATION SUB-EXAMINER CLASS COUNTRY DATE DOCUMENT CLASS INITIAL NUMBER Yes No ΑL Yes No AM Yes No AN Yes No AO Yes No AP OTHER (Including Author, Title, Date, Pertinent Pages, etc.) Kamagami, S., et al., "Penetration enhancement across a model membrane by liposomally entrapped drugs using N,N'-diacylcystine as a bilayer lipid, " Chem. Abstracts 114:457 Abstract No. 214316d, American Chemical Society (1991). AR 2 Kidron, M., et al., "The Absorption of Insulin from Various Regions of the Rat Intestine," Life Sci. 31:2837-2841, Pergamon Press Ltd. (1982). AS <u>9</u> Kiwada, H., et al., "Application of synthetic liposomes based on acyl amino acids or acyl peptides as drug carriers. I. Their preparation and transport of glutathione into the liver," Chem. Abstracts 107: Abstract No. 183493h, American ΑT 9 Chemical Society (1987). DATE CONSIDERED 0S EXAMINER

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 509. line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT



RECEIVED

AÙG 2 8 2001

AUG 2 7 MECH CENTER 1600/2900

| | DOCKET | | |
|-------|---------|------|------|
| 1696. | 0020008 | /RWE | /BEC |
| | | | |

APPLICATION NO.

APPLICANTS Shen et al.

GROUP FILING DATE

| | | | | | May 1, 2001 | 1646 | | |
|---------------------|-----------------|----------|--|--|--|--|--|--------------------|
| | | | | v.s. | PATENT DOCUMENTS | | | |
| EXAMINER INITIAL | | DOCUM | | DATE | NAME | CLASS | SUB- CLASS | FILING DATE |
| | AA | | | | | | _ | |
| | AB | | | | | | <u> </u> | |
| | AC | | | | | | | ļ ———— |
| | AD | | | | | | | |
| | AE | | | | | | | |
| | AF | | | | | | | |
| | AG | | | | | | | |
| | АН | | | | | | | |
| | AI | | | | | | | |
| | AJ | | | | | | | |
| | AK | | | | | | | |
| | | | | FOREI | GN PATENT DOCUMENTS | | | |
| EXAMINER INITIAL | | DOCU | MENT | DATE | COUNTRY | CLASS | SUB- CLASS | TRANSLATION |
| | AL | NOPLE | <u> </u> | | | | | Yea |
| | - | | | | | | | Yes No |
| | AM | | | | | | | Yes |
| | | | | | | | | No |
| | AN | | | | | | | Yes |
| | AO | <i>'</i> | | | | | | No |
| | | | | | | | | Yes No |
| | AP | | | | | Pages etc | ` | |
| | | | OTHER (Inc | luding Author | r, Title, Date, Pertino | ant Pages, etc. | | |
| 10 | AR | 10 | Fibrobla Evolutio Transfor | sts: Historic n and Optimiz mation Assay | ical Transformation in al Background, Assessm ation of the Transform of Established Cell Li aki, eds. IARC Scienti for Research on Cancer | ation Assay Pro nes: Mechanism fic Publication | otocol," I s and Appl | n: ication," T. |
| 18 | AS | 10 | Lee, V.H.L., "Enzymatic Barriers to Peptide and Protein Absorption," Crit. Rev. Ther. Drug Carrier Syst. 5:69-97, CRC Press, Inc. (1988). | | | | | |
| 1 |) _{AT} | 10 | and Prot | (.L., et al., ein Drug Abso nc. (1991). | "Mucosal Penetration E orption," <i>Crit</i> . Rev. Th | Enhancers for F ner. Drug Carri | acilitatio er Syst. (| on of Peptide |
| | //~ | | 1 | | | DATE CO | NSIDERED, | 3/11/05 |
| EXAMINER | /(/ | 2 | <u> </u> | | | | | 7190 |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

· ILUEIVED AUG 2 8 2001 TECH CENTER 1600/2900

TRADE ATTY. DOCKET NO. 1696.0020008/RWE/BEC

AUG APPLICATION NO. 09/845,153

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

APPLICANTS Shen et al.

GROUP FILING DATE

| <u>-</u> | | | | | FILING DATE May 1, 2001 | | 1646 | | |
|---------------------|----------------|-------|------------------------|---|--|---------------|---------|-------------------------------------|--|
| | | | | U.S. | PATENT DOCUMENTS | | | | |
| EXAMINER INITIAL | | DOCUM | | DATE | NAME | CLA | | SUB- CLASS | FILING DATE |
| | AA | | | | | | | | |
| | AB | | | | | | | | |
| | AC | | | | | | | | |
| | AD _ | | | | | | | | |
| | AE | | | | | | } | | |
| | AF | | | | | | | | |
| | AG | | | | | | | | |
| | АН | | | | <u> </u> | | | | |
| | AI | | | | <u> </u> | | | | |
| | . AJ | | | | | | | | |
| | AK | | | | | | | | |
| | | | | FOREIG | IN PATENT DOCUMENTS | | | | Τ |
| EXAMINER INITIAL | | DOCU | MENT | DATE | COUNTRY | CI | ASS | SUB- CLASS | TRANSLATION |
| | AL | NOME | EK | | | | | | Yes No |
| | AM | | | | | | | | Yes No |
| | AN | | | | | | | | Yes No |
| | AO | | | | | | | | Yes No |
| | AP | | | | | | | | Yes No |
| | | | OTHER (Inc | luding Author | , Title, Date, Perti | inent Pages, | etc.) | | |
| P | AR | 11 | Letsinger propertie | r, R.L., et al | l., "Cholesteryl-con ty as inhibitors of " Proc. Natl. Acad. | jugated oligo | onucleo | otides: S man immnu 6556, Nat | ynthesis, odeficieny ional Academy |
| R | AS | 11 | Lowry, O Biol. Ch | owry, O.H., et al., "Protein Measurement with the Folin Phenol Reagent," J. Biol. Chem. 193:265-275, American Society of Biological Chemists, Inc. (1951). | | | | | |
| M | AT | 11 | Martins, enzymati | artins, M.B.F., et al., "Acylation of L-asparaginase with total retention of nzymatic activity," Biochimie 72:671-675, Elsevier Science (1990). | | | | | |
| EXAMINER | J _A | 1 | <u> </u> | <u> </u> | | DAT | E CONS | IDERED | 3/16/05 |

EXAMINER

Draw

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

- AUG 2 8 2001

AUG 2 7 2001 TECH CENTER 1600/29002

FORM PTO-1449

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

communication to Applicant.

ATTY. DOCKET NO. 1696.0020008/RWE/BEC 1 692.445,153

APPLICANTS
Shen et al.

FILING DATE May 1. 2001 GROUP 1646

| | | | | | May 1, 2001 | 1646 | | |
|---|-------------|-------------|----------------------|----------------------------|--|--|---|--|
| | | | | σ. | S. PATENT DOCUMENTS | | | |
| XAMINER NITIAL | | DOCU | MENT ER | DATE | NAME | CLASS | SUB- CLASS | FILING DATE |
| | AA | | | | | | <u> </u> | |
| | AB | | | | | | | |
| | AC | | | | | | | |
| | AD | | | ļ | | | | |
| | AE | | | | | | | - |
| | AF | | | | | | + | |
| | AG | | | <u> </u> | | | | |
| | AH | | | <u> </u> | | _ | | |
| | AI | | | | | | <u> </u> | |
| | AJ | | | | | | | |
| | AK | | | <u></u> | | | | l <u></u> , |
| | | | | FOR | REIGN PATENT DOCUMENTS | | Т - | |
| EXAMINER INITIAL | | DOCU | JMENT BER | DATE | COUNTRY | CLASS | SUB- CLASS | TRANSLATION |
| | AL | | | | | | | Ye N |
| - | | | | | | | | Ye N |
| | AM | + | | | | | | Ye |
| | AN | ļ | | <u> </u> | | | | Ye |
| | AO | | | | | | | Ye |
| | AP | | | | | | | N |
| | | | OTHER (Inc | cluding Aut | hor, Title, Date, Pert | inent Pages, etc.) | | |
| \mathcal{N} | AR | 12 | McConahe Chlorami | y, P.J., an ne-T Method | d Dixon, F.J., "Radioi ," Meth. Enzymol. 70:2 | odination of Prote | eins by t Press, In | he Use of the c. (1980). |
| P | AS | 12 | Mostov, Institut | K.E., and S e of Techno | imister, N.E., "Transo logy (1985). | cytosis, Cell 43: | 389-390, | Massachusetts |
| P | AT | 12 | Müller, cleavage | C.E., et al | ., "Lipophilic disulf: Pharm. 57:41-47, Else | ide prodrugs-synth vier Science Publi | eses and shers B.V | disulfide bon |
| EXAMINER | AX | | | | | DATE CON | SIDERED | 3/6/05 |
| EXAMINER: line throug communicati | h cita | tion i | if not in | considered, conformance | whether or not citation and not considered. | ion is in conforma Include copy of t | nce with | MPEP 609. Dr with next |

APPLICANTS

RECEIVED

AUG 2 8 2001

AUG 2 7 2001 TECH CENTER 1600/2900

APPLICATION NO. DOCKET NO. .0020008/RWE/BEC

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

Shen et al. FILING DATE GROUP

| | | | | | May 1, 2001 | 1 | .646 | |
|---------------------|-----------------|------------|-----------------------------------|--|--|-------------------------------|------------------------------|---------------------------|
| | | | | v.s | . PATENT DOCUMENTS | | | |
| EXAMINER INITIAL | | DOCUMBI | | DATE | NAME | CLAS | SS SUB- CLASS | FILING DATE |
| | AA | | | | | | | |
| | AB | | | | | | | |
| | AC | | | <u> </u> | | | | |
| | AD | | | | | | | |
| | AE | <u> </u> | | | | | | |
| | AF | 1 | | | | +- - | | |
| | AG | | | | | | | + |
| | AH | | | | | | | |
| | AI | | | | | | | |
| | AJ | | | | | | - + - | - |
| | AK | | | | | | | |
| | | | | FORE | IGN PATENT DOCUMENTS | | | |
| EXAMINER INITIAL | | DOCU | UMENT BER | DATE | COUNTRY | CLAS | SS SUB- CLASS | TRANSLATION |
| | AL | 1 | | | | | | Ye: |
| | АМ | $T_{_}$ | | | | | | Ye N |
| | AN | | | | | | | Ye N |
| | AO | 1_ | | | | | | Ye N |
| | AP | T _ | | | | | | Ye N |
| | | | OTHER (In | cluding Autho | or, Title, Date, Perti | nent Pages, e | itc.) | |
| P | AR | 13 | Muranish Releasin Press (19 | ng Hormone and | ., "Lipophilic Peptide d Its Biological Activ | es: Synthesis vity, Pharm. | of Lauroyl T Res. 8:649-6 | hyrotropin- 52, Plenum |
| P | AS | 13 | membrane capsule | kahata, T, and Seki, T., "Functional capsule membranes. 10. pH-sensitive capsu embranes. Reversible permeability control from the dissociative bilayer-coated apsule membrane by an ambient pH change," Chem. Abstracts 102:391 Abstract No. 2733d, American Chemical Society (1985). | | | | |
| A |) AT | 13 | COLL MONG | aa Embruo Cell | al., "Establishment ar ls Sensitive to Postco 3238, American Associa | onfluence inn | TDICION OF DI | TATRION' |
| EXAMINER | '/// | | \ | | | DATE | CONSIDERED | 3/16/05 |

EXAMINER

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP/609. line through citation if not in conformance and not considered. Include copy of this form with next

communication to Applicant.

AUG 2 8 2001 TECH CENTER 1600/2900

ATT. DOCKET NO. TRADE TRADE 1496.0020008/RWE/BEC APPLICANTS

APPLICATION NO 09/845,153

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

Shen et al. GROUP 1646 FILING DATE

| | | | | | May 1, 2001 | 1646 | | |
|---------------------|------------------|----------------|-----------------------------------|--|---|------------------|--|--|
| | | | | v.s. | PATENT DOCUMENTS | | | |
| EXAMINER INITIAL | | DOCUM NUMBE | | DATE | NAME | CLASS | SUB- CLASS | FILING DATE |
| | AA | | | | | | | |
| | AB | | | | | | | |
| | AC | | | ļ | | | | |
| | AD | | | | | | + | |
| | AE | | | | | | + | + |
| | AF | ↓ | | | | | + | + |
| | AG | — | | | | | + | + |
| | AH_ | ↓ | | | | | + | + |
| | AI | ↓ | | | | | + | |
| | AJ | | | | | | 1 | - |
| | AK | ┸— | | PODRIC | ON PATENT DOCUMENTS | | | |
| EXAMINER INITIAL | | DOCUM | | DATE | COUNTRY | CLASS | SUB- CLASS | TRANSLATION |
| | AL | 110 | | | | | | Yei No |
| | | | | | | | | Ye N |
| | AM_ | +- | | + | + | | 1 | Ye. |
| | AN | + | | | | | | Ye. |
| | AO | +- | | | | | | Ye |
| I | AP | | | | | | | N |
| | | , | OTHER (Inc | luding Author | , Title, Date, Perti | nent Pages, etc. |) | |
| P | AR | 14 | Transford Inhibition | | l., "Quantitative and ned C3H Mouse Embryo vision," <i>Cancer Res</i> . | | | |
| M | AS | 14 | Robert, S Microread (1993). | rt, S., et al., "Fatty Acid Acylation of RNase A using Reversed Micelles oreactors," Biochem. Biophys. Res. Commun. 196:447-454, Academic Press, I 3). | | | | |
| p | AT | 14 | Neoglyco | nrotein Usina | crophage-Directed Del Leishmaniasis as the ersity of Chicago Pre | e woder bracase' | oicin Conj " J. Infec | ugated to |
| | يم يل | 'ہےطے | <u></u> | | | DATE COL | NSIDERED | 31/1. |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEF 609. line through citation if not in conformance and not considered. Include copy of this form with next Draw communication to Applicant.

HECEIVED

AUG 2 7 20 MECH CENTER 1600/2900

| | | | | \ <u>~</u> | | W.L. | | I LOTT OLI | Page 15 of 22 |
|---------------------------------------|---------------|--------------|--------------------|---|--|---------------------------------------|----------------|--|---------------|
| | | | | TONTO T | RAUTE 696.0020008/F | IO. | ABPLI 09/84 | CA ION NO 5,153 | |
| | | | 0-1449 | _ | APPLICANTS Shen et al. | | | | |
| INFO | <u>MATION</u> | DISC | LOSURE STA | TEMENT | FILING DATE May 1, 2001 | | GROUP 1646 | · · · · · · · · · · · · · · · · · · · | |
| | | | | U.S. | PATENT DOCUMENTS | l | | | |
| EXAMINER INITIAL | | DOCUI | | DATE | NAME | | CLASS | SUB- CLASS | FILING DATE |
| | AA | | | | | | | | |
| | AB | | | | | | | | |
| | AC | <u> </u> | | | | | | | |
| | AD | | | | | · · · · · · · · · · · · · · · · · · · | | | |
| | AE | | | <u> </u> | | | · | + | |
| | AF | ├ | | | | | | | 1 |
| | AG | - | | | | | | | |
| | AH _ | ┼ | | | | | | | |
| | AI AJ | ┼─╌ | | | | | | | |
| · · · · · · · · · · · · · · · · · · · | AK | + - | | | | | | | <u> </u> |
| | I AN | <u></u> | | FOREI | GN PATENT DOCUMEN | rts | | | |
| EXAMINER INITIAL | | DOCU | MENT SER | DATE | COUNTRY | | CLASS | SUB- CLASS | TRANSLATION |
| · · · · · · · · · · · · · · · · · · · | AL | | | | | | <u> </u> | | Yes No |
| | | | | | | | | | Yes No |
| | AM | - | | | | | <u> </u> | | Yes No |
| | AN | - | | | | | | | Yes |
| | AO | | | | | | | | Yes |
| | AP | | | | | | | | No |
| | | | OTHER (Inc | luding Author | r, Title, Date, Po | ertinent Pag | es, etc.) | | |
| | AR | <u>15</u> | | carrier prop | r, H.PJ., "Poly erties when compl ional Academy of | exed with in | sparin, | rent membr | ane transport |
| P | AS | <u>15</u> | | en, WC., et al., "Enhancement of polypeptide and protein absorption by cromolecular carriers via endocytosis and transcytosis," Adv. Drug Delivery v. 8:93-113, Elsevier Science Publishers B.V. (1992) | | | | | |
| P | AT | 15 | Smith, P. Delivery | L., et al., Rev. 8:253-2 | "Oral absorption 190, Elsevier Scie | of peptides ence Publish | ers B.V. | (1992). | |
| EXAMINER | 7 | /_ | J | | | | DATE CON | SIDERED | 211/18 |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with PEP 609. line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

AT TRANSMENT NO. 1696.0020008/RWE/BEC PPENCATION NO. FORM PTO-1449 APPLICANTS Shen et al. INFORMATION DISCLOSURE STATEMENT GROUP FILING DATE

| | | | | | May 1, 200 | 1 | 1646 | | |
|---------------------------------------|-----|-----------|--------------------------------|---|-----------------------------------|----------------|-------------|---------------|---------------------------|
| | | | | σ.: | S. PATENT DOCUM | KNTS | | | |
| EXAMINER INITIAL | | DOCU | | DATE | NAME | | CLASS | SUB- CLASS | FILING DATE |
| | AA | | | | | | | | |
| | AB | | | | | | | <u> </u> | |
| | AC | | | <u> </u> | | | | | |
| | AD | | | | | | | ļ | - |
| | AE | | | | | | | | |
| | AF | | | | | | | | |
| | AG | | | | | | | | |
| | AH | | | | | | | + | |
| | AI | | | | | | | + | |
| | AJ | | | | | | | + | |
| | AK | | | | | | | | |
| | | | | FOR | BIGN PATENT DOC | UMBNTS | | <u> </u> | T |
| EXAMINER INITIAL | | DOCU | MENT SER | DATE | COUNTRY | | CLASS | SUB- CLASS | TRANSLATION |
| | AL | 1.0 | | | | | | | Ye: |
| , , , , , , , , , , , , , , , , , , , | АМ | | | | | | | | Ye N |
| | AN | | | | | | | | Ye N |
| | | | | | | | | | Ye. |
| | AO | | | | • | | | | Ye N |
| | AP | | | -luddag Auth | or, Title, Date | e. Pertinent l | Pages, etc. | | |
| \mathcal{D} | AR | <u>16</u> | | K., et al. n Jejunum," | , "The Transpor Biochem. Bioph | | t Oligonent | ide Acros | s Adult mic Press, |
| \mathcal{M} | AS | 16 | Innd Baca | Faub, M.E., and Shen, WC., "Polarity in the Transcytotic Processing of Apical and Basal Membrane-Bound Peroxidase-Polylysine Conjugates in MDCK Cells," J . Cell. Phys. 150:283-290, Wiley-Liss, Inc. (1992). | | | | | ng of Apical ells," J. |
| M | AT | 16 | Toth, I Conjugat (1994). | oth, I., "A Novel Chemical Approach to Drug Delivery: Lipidic Amino Acid Onjugates," <i>J. Drug Targeting 2</i> :217-239, Harwood Academic Publishers GmbH 1994). | | | | | |
| EXAMINER | 1/3 | | | | | | DATE CON | SIDERED | dis105 |

EXAMINER

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

HCENTER 1600/2900 AUG 2 / 2001 Page 17 of 22

FORM PTO-1449

INFORMATION DISCLOSURE STATEMENT

| ATTY. BOOKS NO. 1 1696.0020008/RWE/BEC . | ABPLICATION NO. |
|---|-----------------|
| APPLICANTS Shen et al. | |

GROUP 1646 FILING DATE

| L | | | | | May 1, 2001 | 1646 | | | | | |
|---------------------|----|---|--------------|--|--------------------------|-------------|---------------|-------------|--|--|--|
| | | | | v.s. | PATENT DOCUMENTS | | | | | | |
| EXAMINER INITIAL | | DOCT | UMENT BER | DATE | NAME | CLASS | SUB- CLASS | FILING DATE | | | |
| | AA | | | | | | <u> </u> | | | | |
| | AB | ↓ | | | | | | | | | |
| | AC | ↓ | | | | | ļ <u>.</u> | | | | |
| | AD | <u> </u> | | | | | ļ | | | | |
| | AE | <u> </u> | | | | | ļ | ļ | | | |
| | AF | 1 | | | | | | <u> </u> | | | |
| | AG | | | | | | ļ | ļ | | | |
| | AH | ļ | | | | | ļ | ļ <u></u> | | | |
| | AI | | | | · | | 1 | <u> </u> | | | |
| | ΑJ | <u> </u> | | | | | | | | | |
| | AK | <u>.</u> l | | | | | | | | | |
| | | | | FOREIG | N PATENT DOCUMENTS | | .,, | · · | | | |
| EXAMINER INITIAL | | DOC | UMENT BER | DATE | COUNTRY | CLASS | SUB- CLASS | TRANSLATION | | | |
| | AL | | | | | | | Yes No | | | |
| | AM | | | | | | | Yes No | | | |
| | AN | | | | | | | Yes No | | | |
| | AO | | | | | | | Yes No | | | |
| | AP | | | | | | | Yes No | | | |
| | | | OTHER (Inc. | luding Author, | Title, Date, Pertinent P | ages, etc.) | | | | | |
| | AR | Ubuka, T. et al., "Synthesis of disulfides related to glutathione and their detection in tissue," (Ganryu Aminosan) Sulfur Amino Acids 8:153-157, Ganryu Aminosan Kenkyukai (1985). [Article in Japanese] | | | | | | | | | |
| P | AS | <u>17</u> | detection | Touka, T. et al., "Synthesis of disulfides related to glutathione and their detection in tissue," <i>Chem. Abstracts 106:</i> 728, Abstract No. 156843v, American Chemical Society (1987). | | | | | | | |
| 10 | AT | 17 | | chimi, I. et al., "Glutathione derivatives," <i>Chem. Abstracts 73:</i> 359, Abstract o. 56440t, American Chemical Society (1970). | | | | | | | |
| EXAMINER | 1 | 87 | 2 | | | DATE CONS | IDERED 3 | 6/53 | | | |
| t | | | | | | | 1.1 | 7 | | | |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

AUG 2 8 2001)

TECH CENTER 71600/2900

| FORM | PTO- | 14 | 4 | S |
|------|------|----|---|---|
|------|------|----|---|---|

INFORMATION DISCLOSURE STATEMENT

ATTY. DOCKET NO ADPLICATION NO. 1696.0020008/RWE/BEC APPLICANTS Shen et al. GROUP FILING DATE

| | | _ | | | May 1, 200 |)1 | 1646 | | | | |
|---------------------|----|--|--|---|--------------------------------------|--------------------------------|--------------|---------------------|--|--|--|
| | | | | ℧. | S. PATENT DOCUM | ents | | | | | |
| EXAMINER INITIAL | | DOCUM NUMBE | | DATE | NAME | | CLASS | SUB-CLASS | FILING DATE | | |
| | AA | 140 | | | | | | Ath | | | |
| | AB | | | | | | | | 27 2000 | | |
| | AC | | | | | | | | 2007 | | |
| | AD | | | | | | | <u> ' ' ' '</u> | 17:00 | | |
| <u> </u> | AE | <u> </u> | | | | | | | | | |
| | AF | | | | | | | | └── | | |
| | AG | 1 | | | | | | | | | |
| | AH | | | | | | | | | | |
| | AI | 1 | | | | | | | | | |
| | AJ | | | Τ | | | | | | | |
| | AK | 1 | | T | | | | | | | |
| | | | | FOR | EIGN PATENT DOC | :UMENTS | | | т | | |
| EXAMINER INITIAL | | DOCUM | | DATE | COUNTRY | | CLASS | SUB- CLASS | TRANSLATION | | |
| | AL | 1 | | 1 | | | | | Yes No | | |
| | | + | | 1 | | | | | Yes No | | |
| | AM | + | | | | | | | Yes No | | |
| | AN | + | | + | | | | 1 | Yes | | |
| | AO | | | | | · | | + | No Yes | | |
| | AP | | | | | | | | No | | |
| | | | OTHER (In | cluding Auth | hor, Title, Date | e, Pertinent | Pages, etc. |) | | | |
| \mathcal{D} | AR | 18 | Uchimi, I. et al., "Glutathione derivatives," Chem. Abstracts 74:408, Abstract No. 54179m, American Chemical Society (1971). | | | | | | | | |
| m | AS | 18 | Větvička Delivery | ětvička, V., and Fornúsek, L., "Limitations Of Transmembrane Transport In Drug elivery," <i>Crit. Rev. Ther. Drug Carrier Sys</i> t. 5:141-170,CRC Press, Inc. (1988). | | | | | | | |
| D | AT | 18 | Vitetta, and AIDS | , E., "Immun S," J. Clin. | notoxins: New Th . Immunol. 10:15 | nerapeutic Re 5S-18S, Plenu | agents for A | Autoimmunit 90). | y, Cancer, | | |
| EXAMINER | 1 | | | | | | DATE CON | NSIDERED | 3/4/05 | | |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. line through citation if not in conformance and not considered. Include copy of this form with next

communication to Applicant.

AUG 2 3 2001

..- VEIVED AUG 2 8 2001

TECH CENTER 1600/2900 Page 19 of 22

| FORM | PTO- | 1449 | į |
|------|------|------|---|
| | | | |

INFORMATION DISCLOSURE STATEMENT

APPLICATE 09/845,263 09/845,263 09/845,263 ATTY. DOCKET NO. 1696.0020008/RWE/BEC APPLICANTS Shen et al.

GROUP FILING DATE May 1, 2001

| | | | _ | | May 1, 20 | 001 | 1646 | | | | |
|---------------------|-------------------|------|--------------|--|---|----------------------------------|-------------|---------------|--|--|--|
| | | | | σ. | S. PATENT DOCU | MENTS | | | 3 | | |
| EXAMINER INITIAL | | DOCU | | DATE | NAME | | CLASS | SUB- CLASS | FILING DATE | | |
| | AA | | | | | | | | | | |
| | AB | | | | | | | | | | |
| | AC | | | | | | | | | | |
| | AD | | | | | | | ļ | | | |
| | AE | | | | | | | | | | |
| | AF | | | | | | | | | | |
| | AG | | | | | | | | | | |
| | AH | | | | | | | + | | | |
| | AI | | | | | | | ┼ | | | |
| | AJ | | | | | | | | | | |
| | AK | | | | | | | | | | |
| | | | | FOI | REIGN PATENT DO | CUMENTS | | | | | |
| EXAMINER INITIAL | | DOCU | IMENT BER | DATE | COUNTRY | | CLASS | SUB- CLASS | TRANSLATION | | |
| | AL | | | | | | | | Yes No | | |
| | | | | | , | | | Ì | Yes No | | |
| | AM | | | | | | | 1 | Yes | | |
| | AN | 1 | | İ | l | | <u>i</u> | | No | | |
| | - ~~ | + | | | | | | | Yes | | |
| | AO_ | | | | | | | | No | | |
| | | | | | | | l | 1 | Yes No | | |
| | AP_ | | | | hor, Title, Da | - Do-Mannt 1 | Pages etc.) | | | | |
| \mathcal{M} | AR | 19 | Wan, J., | et al., "T | ranscellular P ne Conjugates .ey-Liss, Inc. | rocessing of D in Cultured MD | isulfide-an | d Thioeth | er-Linked J. Cell. | | |
| | AS | 19 | mediated | Wan, J., and Shen, WC., "Brefeldin A and Monensin Enhance Transferrin Receptor- mediated Protein Transport across Epithelial Cells, Pharm. Res. 8:S-4, Plenum Press (1991). | | | | | | | |
| 180 | AT | 19 | l | Wan, J., et al., "Brefeldin A Enhances Receptor-mediated Transcytosis of Transferrin in Filter-grown Madin-Darby Canine Kidney Cells," J. Biol. Chem. 267:13446-13450, American Society for Biochemistry and Molecular Biology, Inc. (1992). | | | | | | | |
| EXAMINER | | 110 | 2 | • | | | DATE CON | SIDERED | 19NS | | |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEP 609. line through citation if not in conformance and not considered. Include copy of this form with next Draw communication to Applicant.

Ĺ

AUG 2 7 2001

10 170 page 20 of 22

AUG 2 8 2001 TECH CENTER 1600/2900 AUG 2 3 2000

| | | | | | ATTY. DOCKERD! | | APPLICATION NO. 09/845,153 | | | | |
|---------------------|----------|--|-------------|---|--|---------------------------|--|---------------|--------------------------|--|--|
| | | | 0-1449 | | APPLICANTS Shen et al. | | | | | | |
| INFOR | MATION | DISC | LOSURE STA | TEMENT | FILING DATE May 1, 2001 | FILING DATE GROUP | | | | | |
| | | | | v.s. | PATENT DOCUMENTS | 3 | | | | | |
| EXAMINER INITIAL | | DOCUM | | DATE | NAME | | CLASS | SUB- CLASS | FILING DATE | | |
| | AA | North | | | | | | | | | |
| | AB | | | | | | | <u> </u> | | | |
| | AC | | | | | | | <u> </u> | | | |
| | AD_ | | | | | | | | | | |
| | AE | | | | | | | | | | |
| | AF | | | | | | | | | | |
| | AG AH | | | | | | | | | | |
| | AI | | | | | | | | | | |
| | AJ | | | | | | | | | | |
| | AK | | | | | | | <u> </u> | <u> </u> | | |
| | | | | FORBIG | N PATENT DOCUMEN | NTS | | 1 | | | |
| EXAMINER INITIAL | | DOCU | | DATE | COUNTRY | | CLASS | SUB- CLASS | TRANSLATION | | |
| | | | | | | | 1 | l i | Yes No | | |
| | AL | + | | | | | | | Yes No | | |
| | AM | | | | - | | | | Yes No | | |
| | AN | | | | | | | | Yes No | | |
| | AO | ┼─- | | | | | | | Yes | | |
| | AP | <u> </u> | | <u></u> | <u></u> | | | | No | | |
| | | | THER (Inc. | luding Author, | Title, Date, P | ertinent Pag | es, etc.) | | | | |
| | AR | <u>20</u> | Anticarci | Tavelow, J., et al., "Bowman-Birk Soybean Protease Inhibitor as an Inticarcinogen," <i>Cancer Res. 43</i> :2454s-2459s, American Association for Cancer Research (1983). | | | | | | | |
| ·/\ | AS | 20 | Intestina | Yodoya, E., et al., "Enhanced Permeability of Tetragastrin across the Rat Intestinal Membrane and Its Reduced Degradation by Acylation with Various Fatty Acids," J. Pharm. Ex. Ther. 271:1509-1513, American Society for Pharmacology and Experimental Therapeutics (1994). | | | | | | | |
| , \(\int \) | AT | 20 | Alpha and | , H., et al., Selective Tr c., (1985). | "Potentiation o ansfer into Lymp | of Enteral Alphatics in R | ats," Pha. | rm. kes. s | Interferon 5:249-250, | | |
| EXAMINER | Λ | | 2 | <u> </u> | | | DATE CON | SIDERED O | 14/15 | | |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEF 609. line through citation if not in conformance and not considered. Include copy of this form with next

communication to Applicant.

AUG 2 8 2001 AUG 2 3 2001 KS
TECH CENTER 1600 P300

AUG 27 2001 21 of 22

| | | | IL | J110- | RADEMAN | | | Begg 21 of 22 | | |
|---|---------|--|-----------------------------------|--|--|--------------------------------|--|---------------------------|--|--|
| | | | | | ATTY. DOCKET NO. 1696.0020008/RWE/BEC APPLICATION NO. 09/849-53; | | | 22 | | |
| | FC | RM PTO | -1449 | | APPLICANTS | | | | | |
| -vr081 | MATTON | DISCIA | OSURE STAT | EMENT | Shen et al. | | | | | |
| INFOR | ·MITON | DIUCA | | | FILING DATE May 1, 2001 | GROU 1646 | ? | | | |
| | | | | U.S. | PATENT DOCUMENTS | | | | | |
| AMINER ITIAL | | DOCUM NUMBE | | DATE | NAME | CLASS | SUB- CLASS | FILING DATE | | |
| | AA | | | | | | | | | |
| | AB | | | | | | | | | |
| | AC | | | | | | | | | |
| | AD | | | | | | | | | |
| | AE | ļ | | | | | | | | |
| | AF | ļ | | | | | | | | |
| | AG | - | | | | | | | | |
| | АН | <u> </u> | | | | | | | | |
| | AI | | | | | | | | | |
| | ΑJ | | | | | | | | | |
| | AK | ــــــــــــــــــــــــــــــــــــــ | | FORBI | ON PATENT DOCUMENTS | | | | | |
| XAMINER NITIAL | | DOCU | | DATE | COUNTRY | CLASS | SUB- CLASS | TRANSLATIO | | |
| | | NUMB | ER | | | | | Y | | |
| | AL_ | | | | | | | Y | | |
| | AM | | | | | | - | Y | | |
| | AN | | | ļ | | | | - Y | | |
| | AO | | | | | | | Y | | |
| | | | | | | | | | | |
| | AP | | THER (Inc | luding Author | , Title, Date, Pertines | nt Pages, etc | .) | | | |
| $\overline{\mathcal{O}}$ | AR | 21 | "Protein, Gove, PhI (1971). | " In: Webste | r's Third New Internati C. Merriam Co. Springfi | onal Dictiona eld, Massachu | ry, Unabr | idged, P.B. A. p. 1823 | | |
| P | AS | 21 | Patent Al Patent O | Patent Abstract of Japanese Publication No. 63246382, obtained from the European Patent Office. | | | | | | |
| $\hat{\mathcal{N}}$ | AT | 21 | Suppleme | Supplementary European Search Report of EP 96 90 3690, mailed March 5, 1998. | | | | | | |
| EXAMINER | | 4 | 10 | | | is in confor | onsidered | 3/9/03 MPEP 609. 1 | | |
| EXAMINER: line throug communicati | th Cita | ation : | I HOU III | considered, w | hether or not citation and not considered. Inc | clude copy of | this form | with next | | |

OIPE SON

RECEIVED

AUG 2 8 2001

TECH CENTER 1600/2900

DATE CONSIDERED

Page 22 of 22

| | | | | | | #: | <u></u> | Page 22 OI 22 | |
|---------------------|---------|--------------|---------------|----------------|--|--|--|---------------|--|
| | | | | | ATTY. DOCKET NO. 1696.0020008/RWE/BEC | 09/84 | CATION NO. 5,153 | | |
| | | | ro-1449 | | APPLICANTS Shen et al. AUG & 7 2001 | | | | |
| INFO | RMATION | DISC | LOSURE STA | <u>TEMENT</u> | FILING DATE May 1, 2001 | GROUP 646 | م حرارت الله | | |
| | | | | | PATENT DOCUMENTS | | -1/6 5 | , | |
| | · | Γ | | 0.8. | T DOCUMENTS | | | | |
| EXAMINER INITIAL | | DOCU NUMB | | DATE | NAME . | CLASS | SUB- CLASS | FILING DATE | |
| | AA | | | | | | | | |
| | AB | | | | | | | | |
| | AC | | | | | <u> </u> | | | |
| | AD | | | | | | | | |
| - | AE | | | | | | ļ | | |
| | AF | | | | | | | | |
| | AG | | | | | <u> </u> | | ļ | |
| | AH | | | | | | | | |
| | AI | | | | | | <u> </u> | | |
| | АJ | | | | | | | | |
| | AK | <u> </u> | | | | | <u> </u> | | |
| | | | | FOREIG | N PATENT DOCUMENTS | | | | |
| EXAMINER INITIAL | | DOCU | MENT SER | DATE | COUNTRY | CLASS | SUB- CLASS | TRANSLATION | |
| | AL | | | | | | | Yes No | |
| | | | | | | | | Yes No | |
| | MA | + | | | | | | Yes | |
| | AN | | | | | | ļ <u> </u> | No | |
| | AO | | | | | | | Yes No | |
| | | 1 | | | | | | Yes No | |
| | AP | <u> </u> | OFFICE (Trac) | luding Author | Title, Date, Pertinent Page | res, etc.) | | | |
| | · · | | JIREK (INC. | Luding Author, | , ,, | | | | |
| | AR | 22 | STN Infor | mation Service | e: File Registry, RN 23130- | 02-1. | | | |
| | AS | 22 | | | | <u> </u> | | | |
| | | | | | | | | | |

EXAMINER: Initial if reference considered, whether or not citation is in conformance with MPEF 609. Draw line through citation if not in conformance and not considered. Include copy of this form with next communication to Applicant.

EXAMINER